CHAPTER 4

PHYSICAL EXAMINATION METHODOLOGY

The first followup examination was provided to four categories of individuals: those who had taken the Baseline questionnaire and Baseline physical examination; those who had been invited to the Baseline events but chose not to participate, only took the questionnaire, or were unlocatable; those Comparisons who had not been invited previously, but who were selected as replacements for Baseline Comparisons noncompliant to this followup examination; and the six newly identified Ranch Hands. As noted in the Baseline Report, all potential study participants were verified as eligible for the AFHS following a detailed review of military personnel records. Replacement individuals were carefully selected, by matching data on the self-perception of health from the noncompliant Comparison (obtained from the telephone survey) with those of the replacement candidate (see Chapter 3 for details).

The followup examination differed logistically from the Baseline examination in one significant way: All structured interval questionnaires were administered at the examination site as contrasted to the in-home interviews conducted at Baseline. The followup examination consisted of the following major elements:

- Interval Questionnaire
- Combat Experience Questionnaire
- Review-of-Systems Questionnaire
- Psychological Testing
- Physical Examination
- Specialized Testing, e.g., Doppler Arterial Studies
- Laboratory Testing
- Psychological and Medical Outbriefings.

Details of the above examination elements were carefully prescribed by the Air Force and set forth as contractual requirements. Clinical innovations or variations were neither desired nor authorized; all proposed examination procedural changes were reviewed in detail by Air Force technical and contractual personnel. An important objective of the technical review was to ensure that bias was not created by any procedural change. The requirement to maintain blind examinations was particularly stringent: The clinical staff was prohibited from knowing or seeking information as to the group identity (Ranch Hand, Comparison) of any participant. At the end of the examination, each participant was asked to note on the critique form whether such information was sought by any member of the clinical or paramedical staff.

EXAMINATION CONTENT

Examination content was designed by the Air Force to emphasize detection of medical endpoints suspected of being associated with exposure to phenoxy herbicides, chlorophenols, or dioxin. In addition, findings in the Baseline examination were used by the Air Force to direct changes in the followup examination (e.g., abnormal pulses at Baseline suggested the need for Doppler measurements at the followup). The general content of the physical examination and psychological test battery is shown in Table 4-1, and the complete laboratory test series is displayed in Table 4-2.

Quality control requirements for both laboratory testing and clinical procedures were extensive. Although details are provided in Chapter 6, the following categories provide an overview of the extent of the quality emphasis. For laboratory testing, single reagent lots and control standards were used when practical, duplicate specimens were routinely and blindly retested, testing overlaps were mandatory when test reagents required change, and fast initial response cumulative statistical techniques (FIR CUSUM) were used to detect rapidly any subtle test drift over time. In addition, 50 specimens from the Baseline serum bank were retested to assess the comparability of laboratory methods. The SCRF clinical team was carefully instructed to assure clinical quality. The quality control elements included: a pretest of the examination process; detailed clinical inspection techniques by SCRF, Science Applications International Corporation (SAIC), and Air Force physicians and personnel; preprinted mark-sense examination forms; clinical quality assurance meetings to detect and correct problems; and blindness of exposure status at the examination. In addition, participant rapport-building techniques were added to boost participation in future followup studies, such as participant critique forms and recreational opportunities afforded to the accompanying family members.

CONDUCT OF EXAMINATIONS

All examinations were conducted at SCRF, La Jolla, California, from May 1985 to March 1986. Except for weeks with national holidays, two groups of participants, averaging about 32 per group, were examined weekly. Midway through the study, NORC recruiters noted that a number of participants refused the examination because of weekday business commitments or because of single-parent responsibilities. Consequently, two special weekend examinations were arranged late in the examination cycle, and many of the former refusals were then able to attend. The examination was identical to the regular 2 1/2-day process, except that it was compressed into 2 days by reducing the number of participants in a group.

The logistics effort required in contacting, transporting, and examining 2,309 study members was formidable. Preexamination contacts consisted of the telephone health survey, telephone recruitment to the examination if necessary, and calls by either the NORC scheduling specialists or by the travel agent to arrange transportation and determine whether special requirements existed (e.g., wheelchair assistance, weekend examination schedule). Once scheduling was reasonably firm, the SAIC logistics coordinator sent each participant a detailed information package outlining dietary requirements, inbriefing schedules, important telephone numbers, a request for medical records, and local maps designating examination-site eating and recreational facilities.

TABLE 4-1.

Elements of the Followup Physical Examination

Elements	Remarks
General Physical Examination	Internist
Neurological Examination	Neurologist
Dermatological Examination	Dermatologist
Electrocardiogram	Resting, 4-Hour Fasting and Nicotine Abstinence
Doppler Peripheral Arterial Blood Flow Studies	4-Hour Nicotine Abstinence
Chest X Ray	
Immunological Studies	50% Random Sample
Skin Test Studies	75% Sample
Psychological Evaluation: Minnesota Multiphasic Personality Inventory (MMPI) Cornell Medical Index Halstead-Reitan Battery	
Patient Outbriefing and Discussion of Individual Results	Medical Diagnostician, Internist, and Ph.D. Psychologist

TABLE 4-2.

Laboratory Test Procedures of the Followup Physical Examination

Clinical Laboratory

Fasting Glucose
Blood Urea Nitrogen (BUN)
Cholesterol
HDL Cholesterol
Triglyceride
Serum Glutamic-Oxaloacetic Transaminase (SGOT)
Serum Glutamic-Pyruvic Transaminase (SGPT)
Gamma-Glutamyl Transpeptidase (GGTP)
Alkaline Phosphatase
Lactic Dehydrogenase (LDH)
Thyroid Stimulating Hormone (TSH)
Initial Cortisol
2-Hour Cortisol

Prothrombin Time
Quantitative Immunoglobulins
Complete Blood Count (CBC)
Leuteinizing Hormone (LH)

2-Hour Postprandial Glucose
Creative Phosphokinase (CPK)
Total Bilirubin
Direct Bilirubin
Total Protein
Protein Electrophoresis
Routine Urinalysis
T_3 % Uptake
T_4
Testosterone
Hepatitis B Surface Antigen
Hepatitis B Surface Antibody
Follicle Stimulating Hormone (FSH)

Rapid Plasma Reagin (RPR)
Porphyrins (Mayo Clinic)
Sedimentation Rate

Immunological Laboratory

Cell Surface (Phenotype) Analyses
Lymphocyte Mitogen Stimulation Assays
Mixed Lymphocyte Culture (MLC)
Natural Killer Cell Assay by Specific Cellular Cytotoxicity Using K-562 Target Cells

Natural Killer Cell Assay (Using Interferon) by Specific Cellular Cytotoxicity Using K-562 Target Cells

The logistical flow of the entire examination process was complex. Figures 4-1 and 4-2 outline participant flow for the first 2 examination days. As depicted in these figures, each group of participants (generally containing equal numbers of Ranch Hands and Comparisons) was transported early in the morning to SCRF on the first 2 days in a fasting state; tobacco, alcohol, and coffee abstinence were also required. Following initial inbriefing and blood draw on the first day, each participant was randomly assigned to the examination group or to the psychological testing group. On the second day, these groups were reversed. After randomization, each member was given an individualized 3-day schedule outlining his medical, interviewing, and laboratory appointments. The schedule carefully noted the specific required periods of fasting and tobacco abstinence (see Figures 4-1 and 4-2 for generalized periods in relation to ECG and Doppler testing). Each individual was reminded of the fact that all aspects of the examination were strictly voluntary, and that refusals would be honored without question. Both general and specific consent forms (e.g., skin biopsy), approved by the Air Force, were explained in detail.

In contrast to the Baseline examination, great reliance was placed upon each individual to find the appropriate clinic area at his scheduled time. This approach had great appeal to this self-reliant population as evidenced by critique feedback. Throughout the examination day, generous time was provided for waiting-room activities, i.e., renewal of past friendships, discussions of the Vietnam War, consumption of refreshments when permitted, and completion of paperwork. Day 3 of the examination was largely spent in finishing up the specialty examinations and receiving the outbriefings from a psychologist and medical diagnostician. Only upon completion of these important debriefings were the participants paid their stipend, reimbursed for travel expenses, and transported to the airport.

As noted previously, the SCRF clinical team was hand-picked for participation in this project. In total, 15 board-certified physicians in internal medicine, neurology, and dermatology participated in the general, specialty, and diagnostic examination. To reduce observer variability, turnover in the clinical or paramedical staffs was minimized during the 9 months of examinations. One SCRF physician served as the Project Medical Director, responsible for the scheduling, conduct, and quality control of the examinations. All examining physicians were introduced to the mark-sense examination forms during the pretest examination. The layout of the form was designed to parallel the flow of the clinical examination so as to minimize recording errors. Because data transcription was not permitted, each physician was responsible for filling in the bubbled form. To a large extent, these mark-sense forms and subsequent quality control were the primary reason for a remarkably clean data set. Two examples of the mark-sense forms are presented as Figures 4-3 and 4-4; a complete set of forms is provided in Appendix C.

For the first followup, the special testing included Doppler tests, delayed hypersensitivity skin tests, and immunological tests. Doppler measurements were obtained on all participants by highly experienced technicians; results were recorded and Polaroid photographs were taken of representative oscilloscope displays. As previously noted, considerable emphasis was placed upon tobacco abstinence prior to Doppler evaluations. Skin tests for four antigens were administered in a standardized manner: Candida (1:1,000 weight/volume, 0.1 ml intradermal), mumps (2 complement-fixing units), Trichophyton (1:1,000 weight/volume, 0.1 ml intradermal), and

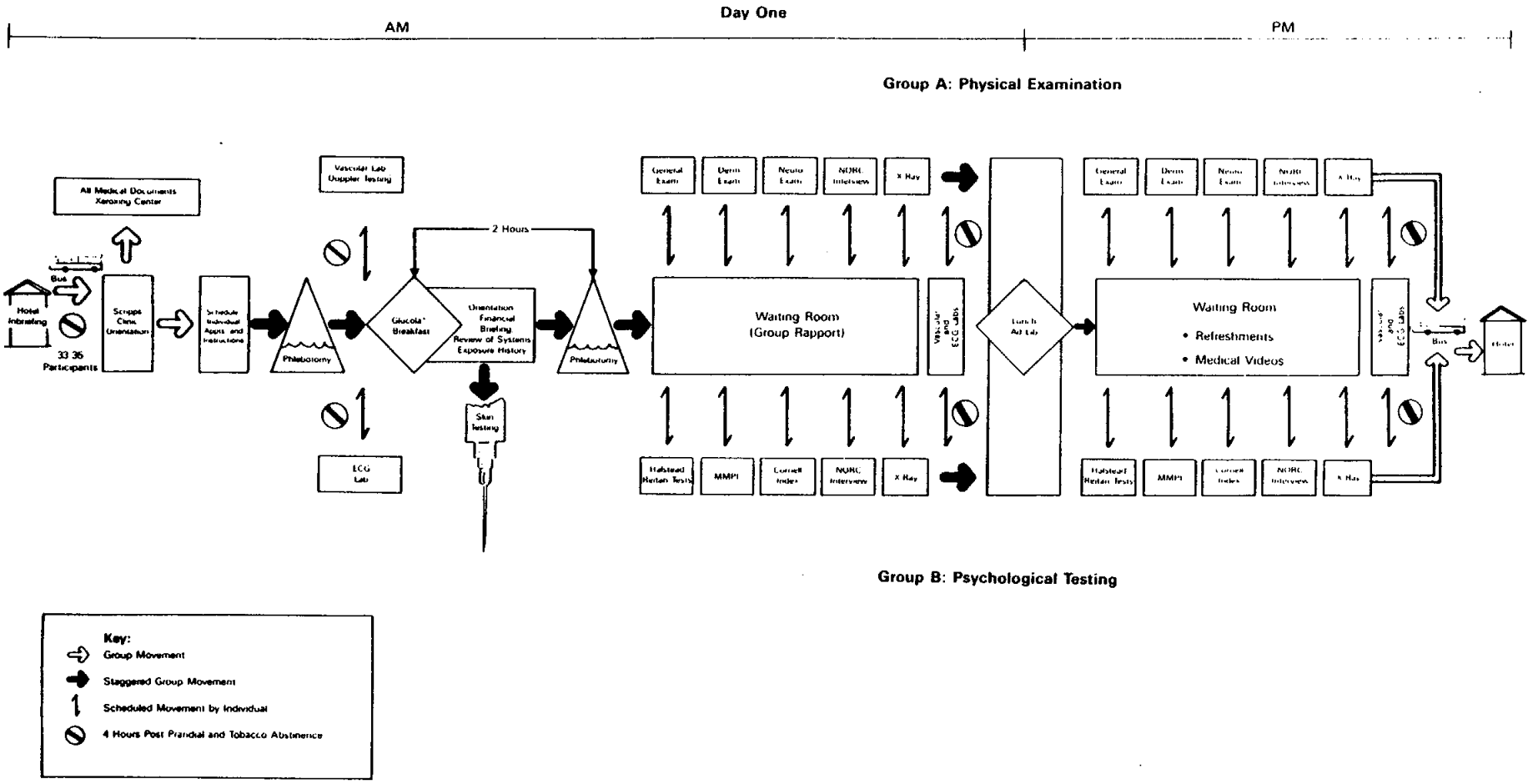

Figure 4-1.
Flow Diagram of Day One Followup Interview and Physical Examination